

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
7 February 2002 (07.02.2002)

PCT

(10) International Publication Number  
**WO 02/010750 A3**

(51) International Patent Classification<sup>7</sup>: **G01N 33/50**,  
C07K 14/435, G01N 21/64, C12N 15/62

(74) Agents: **QUINE, Jonathan, Alan et al.**; The Law Of-  
fices of Jonathan Alan Quine, P.O. Box 458, Alameda, CA  
94501 (US).

(21) International Application Number: PCT/US01/24182

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,  
ZW.

(22) International Filing Date: 31 July 2001 (31.07.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/222,056 31 July 2000 (31.07.2000) US  
60/244,764 31 October 2000 (31.10.2000) US

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,  
TG).

(71) Applicant (*for all designated States except US*): **MAXY-  
GEN, INC.** [US/US]; 515 Galveston Drive, Redwood City,  
CA 94063 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **MINSHULL,**  
**Jeremy** [GB/US]; 842 Hermosa Way, Menlo Park, CA  
940251 (US). **DAVIS, S., Christopher** [GB/US]; 18  
Church Street #103, San Francisco, CA 94114 (US).  
**WELCH, Mark** [US/US]; 25 Montalban Drive, Fremont,  
CA 94536 (US). **RAILLARD, Sun, Ai** [CH/US]; 964  
Trophy Drive, Mountain View, CA 94043 (US). **VOGEL,**  
**Kurt** [US/US]; 4151 #D, El Camino Way, Palo Alto, CA  
94306 (US). **KREBBER, Claus** [DE/US]; 1935 Rock  
Street #1, Mountain View, CA 94043 (US).

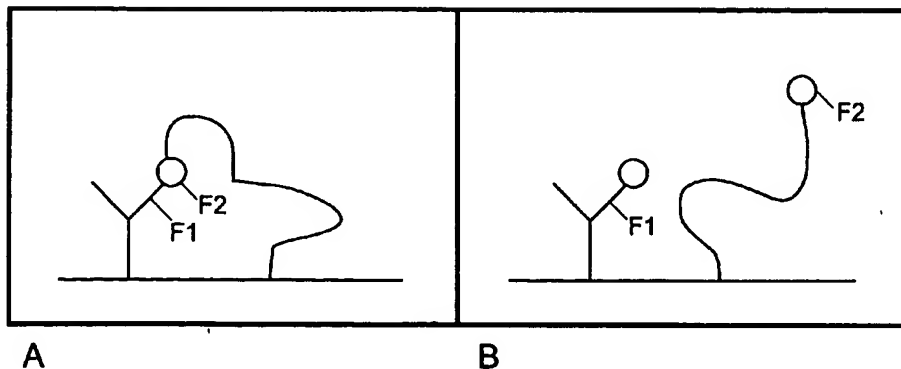
Published:

— *with international search report*  
— *before the expiration of the time-limit for amending the  
claims and to be republished in the event of receipt of  
amendments*

(88) Date of publication of the international search report:  
10 July 2003

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: BIOSENSORS, REAGENTS AND DIAGNOSTIC APPLICATIONS OF DIRECTED EVOLUTION



(57) Abstract: Methods for sensing test stimuli using arrays of biopolymers are provided. Libraries of biopolymers, such nucleic acid variants, and expression products encoded by nucleic acid variants are provided. Reusable library arrays, and methods for their use are provided.

# INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 01/24182

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 GO1N33/50 C07K14/435 G01N21/64 C12N15/62

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 GO1N C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 949 269 A (SYMBIOSIS GMBH) 13 October 1999 (1999-10-13) abstract figure 1 example 1 claims 1-7	67-69, 73,74
X	WO 98 27104 A (UNIV YALE ;BREAKER RONALD R (US)) 25 June 1998 (1998-06-25) abstract	38,73,74
	---	
	---	
	--- --	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*A\* document member of the same patent family

Date of the actual completion of the international search

14 April 2003

Date of mailing of the international search report

08/05/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Weijland, A

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/24182

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MIYAWAKI A ET AL: "FLUORESCENT INDICATORS FOR CA<sup>2+</sup> BASED ON GREEN FLUORESCENT PROTEINS AND CALMODULIN" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 388, no. 6645, 28 August 1997 (1997-08-28), pages 882-887, XP002058386 ISSN: 0028-0836 abstract figure 1A</p>	1,14,17, 38,52,59
X	<p>MITRA ROBI D ET AL: "Fluorescence resonance energy transfer between blue-emitting and red-shifted excitation derivatives of the green fluorescent protein." GENE (AMSTERDAM), vol. 173, no. 1, 1996, pages 13-17, XP002238134 ISSN: 0378-1119 abstract</p>	25,38,52
A	<p>BAIRD G S ET AL: "Circular permutation and receptor insertion within green fluorescent proteins" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 96, no. 20, 28 September 1999 (1999-09-28), pages 11241-11246, XP002187230 ISSN: 0027-8424 the whole document</p>	1-126
A	<p>TSIEN R Y: "THE GREEN FLUORESCENT PROTEIN" ANNUAL REVIEW OF BIOCHEMISTRY, PALTO ALTO, CA, US, vol. 67, 1998, pages 509-544, XP000946725 ISSN: 0066-4154 the whole document</p>	1-126

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 01/24182

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0949269	A	13-10-1999	EP 0949269 A1	13-10-1999
WO 9827104	A	25-06-1998	AU 724627 B2	28-09-2000
			AU 5810798 A	15-07-1998
			EP 0958303 A1	24-11-1999
			JP 2002514913 T	21-05-2002
			WO 9827104 A1	25-06-1998